REMARKS

Claims 1-4 and 6-22 are pending in the application. Claims 1-4 and 6-22 are rejected. Claims 1, 9, and 16 are presently amended. In view of the amendments and the discussion below, it is submitted that the application is in condition for allowance.

Claim Rejections 35 U.S.C. § 103(a)

The Examiner has maintained the rejections of claims 1-4 and 6-22 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,586,478 (Ackman) in view of U.S. Patent No. 6,264,981 (Zhang). The Examiner states that Ackman teaches compositions for improving sleep, which include methadone, and Zhang teaches a transmucosal drug dosage form (e.g., a lollipop) for oral mucosal delivery of a pharmaceutical agent. The Examiner then suggests that it would have been obvious to one of ordinary skill in the art to use the drug dosage form of Zhang to deliver the composition of Ackman, thereby delivering the sleep-promoting composition including methadone transmucosally. In view of the claims as presently amended, Applicants respectfully disagree.

Applicants had previously argued over the combination of Ackman and Zhang when responding to the previous Office Action (dated April 9, 2007). More specifically, Applicants had previously amended each of independent claims 1, 9, and 16 to recite that the claimed formulation was "nonsedative" and was effective to treat

"acute pain." Applicants had then generally asserted that these limitations avoided Ackman (at least because Ackman teaches a composition for promoting sleep), and Zhang (at least because Zhang teaches compositions having actions opposite to methadone).

In presently maintaining the rejections of the pending claims as obvious over Ackman in view of Zhang, the Examiner generally asserts (1) that Ackman does not teach methadone to be sedative, and (2) that Applicants arguments over Zhang are immaterial because Zhang is only used for its teaching of a lollipop drug delivery vehicle. More specifically, the Examiner makes four specific assertions in response to Applicants' previous arguments. First, the Examiner states that Applicants' only evidence for Ackman's disclosure of a sedative is column 4, lines 19-32 of Ackman, which recite sedatives as a class of established drugs for sleep disorders (specifically, sedative antidepressants). However, the Examiner states that methadone is taught by Ackman to be in a class of opioids, rather than the class of sedative antidepressants. Second, the Examiner now cites U.S. Patent No. 5,919,781 (Baker) as teaching that withdrawal syndrome in opiate addicts, which includes sleep disturbances, is avoided by increasing doses of methadone as the opiate is withdrawn. Third, the Examiner states that one of ordinary skill in the art would only use the drug delivery vehicle of Zhang to deliver the composition of Ackman (rather than using any active ingredients recited in Zhang). And finally, as to the recitation of "acute pain," the Examiner merely states that

the motivation to combine need not be Applicants' motivation to invent (citing *In re* Dillon 16 USPQ 2d 1897 (Fed. Cir. 1990)).

Even taking into account the Examiner's assertion that only the drug delivery vehicle of Zhang would be used to deliver the composition of Ackman (without using any recited pharmaceutical agents of Zhang), Applicants again respectfully disagree with the rejection of claims 1-4 and 6-22 as obvious over Ackman in view of Zhang. In particular, in this response Applicants assert that Ackman teaches away from the presently claimed invention. Thus, it would not be considered by one of ordinary skill in the art.[1]

To that end, Applicants note that each of independent claims 1, 9, and 16 have been amended to recite "an analgesic dosage formulation effective to . . . avoid a sedative effect." Thus, all of the claims of the present application are directed to, and recite, a formulation which avoids a sedative effect. Each of the independent claims also recites that this formulation that avoids a sedative effect includes methadone. Support for the presently amended claims may be found at least at page 2, lines 3-7; page 3, lines 13-15; page 9, line 23 through page 10, line 5; page 10, lines 5-7; and page 20, lines 19-21. There, the application describes that when opioids are used to

[1] Thus, the thrust of Applicants' arguments in this Response are directed primarily to an analysis of the composition disclosed by Ackman, and particularly in conjunction with the present claims recitations regarding sedative properties of compositions (or lack thereof). However, while the focus here is not on the "acute pain" limitations of the claims, this is not an acknowledgement or admission of the Examiner's position with respect to the recitation of "acute pain."

treat pain, patients generally become tolerant to the analgesic effects of the opioid and thus require escalation of the dosage amounts of the opioid in order to maintain the desired analgesic effects. This results in increased side effects, one of which is sedation. However, tolerance to the analgesic effects of methadone develops more slowly than with other commonly used opioids. Thus, it follows that since tolerance develops more slowly with methadone, the escalation of dosage amounts (as with other opioids) is not necessary, and so any sedative effects are avoided.

And so, the claimed invention of the present application is a formulation that avoids a sedative effect. Particularly, the presently claimed composition does not induce, promote, or improve sleep. Quite the contrary, the present composition, as recited in the claims, is explicitly the opposite of any composition that would improve sleep.

Ackman is explicitly directed to a composition for improving sleep In fact, as pointed out by the Examiner, that is the very title of Ackman. The composition of Ackman includes a nitric oxide mimetic and an established drug for sleep disorders. Applicants submit that one skilled in the art would not look to Ackman for a formulation including methadone that avoids a sedative effect (as is disclosed and claimed by the present application), due to Ackman explicitly describing a composition for improving sleep. As opposed to Ackman, when the formulation (including methadone) of the present application is used for pain treatment, sedation is reduced. (See Declaration,

paragraph 11; submitted with Response dated July 9, 2007). Thus, a dosage form including methadone for the treatment of sleep disorders (as described by Ackman) would not be a viable treatment option for avoiding a sedative effect, as is the presently claimed invention.

More specifically, and as argued generally above, the entire teaching of Ackman is explicitly opposite to, and directly contrary to, a formulation (including methadone) that avoids a sedative effect. In summary, Ackman describes that sleep disorders have large negative impacts on people's lives (column 1, lines 34-37); and that there are over 70 sleep disorders that are diagnosed and treated by healthcare providers (column 1, line 38 et seq.). Sleeping pills have been used to treat such disorders, but there are many limitations and risks to their use (column 2, lines 25-30). For example, development of tolerance to a drug's effect may rapidly render the drugs ineffective (column 2, lines 43-45). Opioids such as methadone have been prescribed for sleep disorders, but they also have the undesirable side effect of being potentially addictive (column 2, lines 59-64). And so, Ackman states that there is a need for a drug treatment to improve sleep, but which avoids such undue side effects (column 3, lines 3-6). To accomplish this, Ackman teaches a method of improving sleep via a NO-mimetic administered either alone, or in combination with other NO-mimetics or an established drug for sleep disorders (such established drugs for sleep disorders including methadone) (column 3, line 64 through column 4, line 32).

Thus, Applicants submit that that Ackman would not be looked to by one skilled in the art because it discloses a different drug (a combination of a nitric oxide mimetic and other drug, possibly methadone) for a different indication, specifically the improvement of sleep. The particular combination drug disclosed by Ackman consists specifically of a drug designed to maximize any sedative effect methadone may have with the intent of inducing sleep. That is the very opposite of, and teaches directly away from the presently claims invention, which recites a formulation that avoid a sedative effect. As a result, Applicants submit that a person skilled in the art seeking to prepare a formulation for analgesia that does not induce sleep (as is the presently claimed invention) would never look to a reference that is explicitly directed toward improving sleep (i.e., Ackman).

As described previously, each of independent claims 1, 9, and 16 recites a formulation that provides analgesia for the treatment of acute pain, and in doing so, avoids sedative effects or otherwise inducing sleep. The Examiner seeks to reject these claims as obvious by pointing to a reference (Ackman) that is specifically directed to (as acknowledged by the Examiner) inducing or improving sleep. The composition of Ackman is not used to treat acute pain; it is specifically used to induce sleep, and includes a nitric oxide mimetic (possibly in combination with methadone) specifically to enhance sleep-inducing properties. Applicants submit that Ackman, which teaches a combination drug specifically designed to enhance sleep, teaches away from and would

not be considered by one of ordinary skill in the art when considering a drug that treats acute pain at dosages that avoid any sleep-inducing or improving properties.

In view of the above, Applicants request withdrawal of the rejection of claims 1-4 and 6-22 under 35 U.S.C. §103(a) as unpatentable over Ackman in view of Zhang.

Claim Rejections 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1-4 and 6-22 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner points to Applicants' previous amendments to the claims to include the recitation of the composition as "nonsedative." The Examiner states that nowhere in the specification do Applicants disclose the adjective "nonsedative." The Examiner states that at best, Applicants disclose treating a sedative effect.

Applicants note that each of independent claims 1, 9, and 16 have been amended to recite that the dosage formulation of the composition is "an analgesic dosage formulation effective to treat acute pain and avoid a sedative effect." Thus, all of the claims of the present application are directed to, and recite, a composition including methadone for the treatment of acute pain, which avoids a sedative effect. Support for this amendment may be found at least at page 2, lines 3-7; page 3, lines 13-15; page 9, line 23 through page 10, line 5; page 10, lines 5-7; and page 20, lines 19-21. There, as described above, the application describes that when opioids are used to

treat pain, patients generally become tolerant to the analgesic effects of the opioid and thus require escalation of the dosage amounts of the opioid in order to maintain the desired analgesic effects. This results in increased side effects, one of which is sedation. However, tolerance to the analgesic effects of methadone develops more slowly than with other commonly used opioids. Thus, it follows that since tolerance develops more slowly with methadone, the escalation of dosage amounts (as with other opioids) is not necessary, and so any sedative effects are avoided.

In view of the above, Applicants respectfully request a withdrawal of the rejection of claims 1-4 and 6-22 under 35 U.S.C. § 112, first paragraph.

Conclusion

For the foregoing reasons, it is submitted that all claims are patentable, and a Notice of Allowance is respectfully requested.

No fee is believed due. Any deficiencies or credits necessary to complete this communication should be applied to Deposit Account No. 23-3000.

The Examiner is invited to contact the undersigned attorney with any questions or remaining issues.

Respectfully submitted,
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